UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,748	10/06/2006	Joseph R. Garlich	050990.0201.02USPC	3652

27148 7590 01/06/2009

POLSINELLI SHALTON FLANIGAN SUELTHAUS PC
700 W. 47TH STREET
SUITE 1000
KANSAS CITY, MO 64112-1802

EXAMINER	
RAE, CHARLESWORTH E	

ART UNIT	PAPER NUMBER
1611	

MAIL DATE	DELIVERY MODE
01/06/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,748	GARLICH ET AL.	
	Examiner	Art Unit	
	CHARLESWORTH RAE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *1-4 and 7-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5 and 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 09/24/08, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

It is noted that a prior art search did not reveal any prior art references teaching applicant's elected compound, SF1740, wherein R is NHCOCH2OPh (see specification, page 77, Table 26). Thus, the search was expanded to include the compound species wherein R1 is NR5R6, wherein R5 and R6 are independently hydrogen.

This action is made final.

Allowable Subject Matter

As indicated above, a search of applicant's elected compound failed to reveal any prior art references. Thus, claims reciting applicant's elected compound is found to be directed to allowable subject matter.

Status of the Claims

Claims 1-12 are currently pending in this application.

Claims 1-4 and 7-12 are withdrawn for examination purposes for being directed to non-elected subject matter.

Claims 5-6 are under examination.

Miscellaneous

It is noted that the term "cerebrovaxcular" is recited on page 45, line 4, of the instant specification, which appears to be a typographical error. It is suggested that applicant review the specification for typographical errors and correct any typographical error by way of an amendment to the specification as required.

REJECTION

Claim rejections – 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

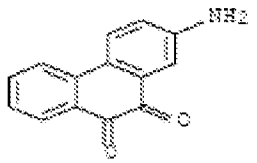
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 5 is rejected under 35 USC 102(b) as being anticipated by Chapdelaine et al. (US Patent Application Pub. No. 2003/0207812 A1) as evidenced by Ross (Ross. Atherosclerosis- An inflammatory disease. New Engl J Med. 1999;340(2):115-126).

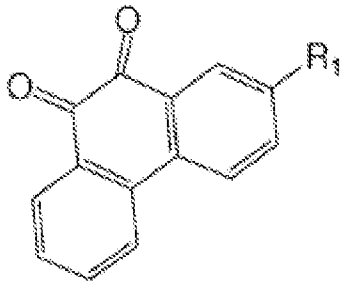
Chapdelaine et al. teach the below compound which is identical to applicant's compound species wherein R1 is NR5R6 wherein R5 and R6 are independently hydrogen (paras 0008 and 0023).

RN 36043-49-9 HCAPLUS
CN 9,10-Phenanthrenedione, 2-amino- (CA INDEX NAME)



IT 604-95-5P 345630-42-4P
(preparation of phenanthrenedione derivs. as CD45 inhibitors)
RN 604-95-5 HCAPLUS
CN 9,10-Phenanthrenedione, 2-nitro- (CA INDEX NAME)

It is noted that instant claim 5 recites the below core structure:



wherein,

R^1 represents H, NO_2, NR^5R^6, halogen, cyano, alkyl, alkylaryl, carbonyl, carboxy, COR^2, or $CONR^5R^6$;

R^2 and R^3 independently represent H, C^1-C^4 alkyl, aryl, or alkylaryl;

R^4 represents H, C^1-C^6, alkyl, aryl, alkylaryl, SO_2R^2, $NHSO_2R^2$, $NHCOR^2$, $NHCO_2R^2$, $N=CR^2R^3$, or NR^5R^6;

R^5 and R^6 independently represent H, C^1-C^4 alkyl, aryl, alkylaryl, $(CH_2)_nCOXR^2$, $(CH_2)_nXR^2$, $(CH_2)_nCO(CH_2)_nXR^2$, SO_2R^2, $(CH_2)_nCO(CH_2)_nCOXR^2$, or $(CH_2)_nXR^2$;

m=0-3;

n=0-3; and

X represents CR^2R^3, O, or NR^2.

Chapdelaine et al. also teach compositions and methods of treatment comprising administering said compounds for treating T-cell mediated conditions such as immunologically related diseases, autoimmune disorders and organ graft rejection (see abstract; paras. 0002-0007, and reference claim 7) and T-cell activation is also involved with damage to normal tissue attributable to heart disease from atherosclerosis as evidenced by Ross (Ross. Atherosclerosis- An inflammatory disease).

Ross is added as an evidentiary reference only to show that T lymphocytes mediate atheroslerosis which is known to damage normal tissue of the heart and therefore atherosclerosis is reasonably considered to be a T-cell mediated condition. Ross teaches that atherosclerosis occur principally in large medium-sized muscular

arteries and can lead to ischemia of the heart (page 115, col. 1, second para.). Ross also teaches that the earliest type of atherosclerotic lesion involves a pure inflammatory lesion, consisting only of monocyte-derived macrophages and T lymphocytes and that endothelial dysfunction is mediated by specific subtypes of T lymphocytes at every stage of the disease (page 115, col. 1, last para.; and col. 2, second para.).

It is noted that Ross is only being relied upon as an evidentiary reference.

It is noted that the instant specification discloses that the invention enables patients to be treated with a small molecule to inhibit PTEN for augmenting immunity (page 45, lines 2-6). Also, applicant discloses that PTEN inhibitors augment immunity (see specification, page 45, lines 2-6).

With respect to the preamble, Chapdelaine teach compounds that are useful for treating T-cell related disorders and the instant claims are also directed to methods of treating a patient suffering from damage to normal tissue attributable to heart disease which is known to caused by atherosclerosis, which is mediated by **T-cell activation** as evidenced by the teaching of Ross. Hence, one would reasonably expect that administration of the identical instantly claimed compound species as taught by Chapdelaine in an amount effective in treating the identical patient population (= T-cell mediated conditions) would be also be effective in treating the genus of T-cell disorders, including the instantly claimed patient population suffering from damage to normal tissue attributable to heart disease (i.e. atherosclerosis-related heart disease), since Chapdelaiene provides a general teaching of a method of treating T-cell conditions. Thus, since the cited art teaches the identical instantly claimed compound species to

treat the identical instantly claimed population (T-cell mediated conditions) as evidenced by the teaching of Ross that atherosclerosis, and atherosclerosis, which is a major risk factor for heart disease, is also mediated by T-lymphocytes, one would reasonably expect that the administration of the same drug the same population (= T cell mediated conditions) would exhibit the same therapeutic effects. Thus, the preamble is anticipated by the prior art.

For the above reasons, claim 5 is anticipated by the prior art.

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chapdelaine et al. (US Patent Application Pub. No. 2003/0207812 A1) as evidenced by Ross (Ross. Atherosclerosis- An inflammatory disease. New Engl J Med. 1999;340(2):115-126).

The above discussions of Chapdelaine et al. and Ross are incorporated by reference.

Based on the teaching of Chapdelaine et al. one would not immediately envisage administering the instant claimed "PTEN inhibitor … prior to, together with, or after a treatment for a disease suffered by the patient."

It would have been obvious to a person of skill in the art at the time the invention was made to administer the instant claimed PTEN inhibitor compound species prior to, together with, or after a treatment for a disease suffered by the patient to control any coexisting diseases. One would have been motivated to do so because patients with heart disease usually suffer from other coexisting problems such as hypertension in addition to atherosclerosis and therefore the only reasonable options available for administering the PTEN inhibitor would be prior to, together with, or after the treatment (e.g. anti-hypertensive treatment) for the other coexisting diseases (e.g. hypertension).

Further, it is examiner's position that it is routine in the medical art to treat a patient with heart disease with two or more therapeutic modalities (e.g. angioplasty and drug therapy, or two or more drugs) and that it would have been within the scope of knowledge and skill of an artisan in the art to administer the instant claimed compounds together with or after another therapeutic modality depending on factors such as the patient's age, severity of heart disease, or the presence of other coexisting disorders, in order to minimize drug-induced side effects.

Thus, it would have been obvious to a person of skill in the art at the time the invention was made to create the instant claimed invention with reasonable predictability.

Response to applicant's arguments/remarks

In response to applicant arguments that the cited art fails to establish a prima facie case of obviousness, it is the noted that this argument is rendered moot by the new basis of rejection under 102(b).

With respect to the rejection under 103(a), to the extent that Chapdelaine et al. teach the identical instantly claimed compound species, wherein R1 is NR5R6, and wherein R5 and R6 are hydrogen, applicant's argument regarding the motivation to modify the general core structure as taught by Chapadelaine is also rendered moot. Further, as discussed above, one would reasonably expect that the administration of the identical drug to the same population (patients suffering with T-cell mediated conditions) would have the same therapeutic effects. Thus, the rejection under 103(a) is deemed to be proper.

Relevant Art of Record

The below cited art made of record and relied upon is considered pertinent to applicant's invention and is cited to show the general state of the art regarding the therapeutic utility of PTEN inhibitors.

Durden (US Patent 6,777,439) teaches PTEN inhibitors and methods of using said compounds for treating aberrant angiogenesis associated with several diseases, including cancer, autoimmune diseases, coronary artery diseases, and atherosclerosis (col. 2, lines 44-54).

Conclusion

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-

6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau, can be reached at 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

10 December 2008

/C. R./ Examiner, Art Unit 1611.

/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611